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RING BAG

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(54) Title: CENTRIFUGE AND CONTAINER SYSTEM FOR TREATMENT OF BLOOD AND BLOOD COMPONENTS		
(57) Abstract		
<p>A centrifuge with an associated container system in the form of cassettes for separation and/or treatment of blood or blood components. The centrifuge comprises a rotor (1) having a central compartment in the form of a tubular shaft cavity (6) extending concentrically with the axis of rotation of the rotor and an annular separation compartment (5) which is arranged around said cavity at the upper part thereof. A first container system to be arranged in said rotor and intended for e.g. washing of blood cells, comprises a round bag (13) and two or more flexible secondary containers (14, 15) connected thereto, of which at least one contains a treatment liquid, and a tubular sleeve (17) adapted to the shaft cavity of the rotor. The secondary containers are arranged standing in the sleeve resting against each other, and the round bag is mounted on a projecting flange (22) at the upper part of the sleeve. A second container system to be arranged in said rotor and intended for e.g. separation of a thrombocyte suspension differs from the above by the fact that the sleeve (39) has a smaller diameter than the shaft cavity of the rotor and is adapted to be centred in the centre of the cavity. An initially empty secondary container (41) for receiving the separated components from the round bag is arranged in the centred sleeve.</p>		

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Centrifuge and container system for treatment of blood and blood components

The invention relates to a centrifuge for separation and/or treatment of blood or blood components, comprising a rotor having a central compartment and an annular separation compartment, which are arranged concentrically with the axis of rotation of the rotor and are adapted to accommodate a container system comprising a round bag and one or more secondary containers connected thereto, the separation compartment being adapted to accommodate the round bag and the central compartment being adapted to accommodate the secondary containers, and the centrifuge further comprising means for reducing, in operation, the volume of the separation compartment in order to displace a separated fraction from the round bag to a secondary container in the central compartment.

The invention also relates to a container system to be arranged in the centrifuge according to the invention.

By round bag is below meant an essentially annular flexible container, which can be produced, for instance, by welding together superimposed plastic films along an outer annular edge and an inner annular edge. The annular container can, in the same way as described in WO 95/01842, be cut off and the thus-formed opposite ends sealed. These opposite ends are arranged in an overlapping manner when the round bag is mounted in the centrifuge or on a cassette, thereby giving the round bag the shape of a truncated cone.

US Patent 5,114,396 discloses a method and a container system for washing blood cells by using a centrifuge of the type mentioned by way of introduction. In this prior-art container system, use is made of the central part inside the round bag as a secondary container, and a continuous unit is obtained, which essentially is oriented in a horizontal plane. When large volumes of liquid are to be handled in the secondary containers, this container system requires a large rotor diameter.

International Patent Application WO 95/01842 discloses a container system which in a corresponding manner utilises the central part inside the round bag as a secondary container. In this case, the round bag is shortened by letting two opposite sealed ends of the ring overlap in connection with the mounting of the round bag on a rigid centre part, thereby obtaining the shape of a truncated cone. The secondary container is pressed into a cavity in the rigid centre part. The cavity has a smaller

diameter than the secondary container, and its radially outer parts are folded along the walls of the cavity. In this way, the entire system obtains a small diameter and can be accommodated in a correspondingly small rotor. Especially when separating sensitive cell suspensions, e.g. platelets, this system has great advantages since

5 the separation must be effected with a certain amount of caution and the cell suspension is not allowed to be exposed to high G fields for long periods. However, the system is suited above all for separations where the secondary containers are initially empty and can easily be mounted in a deformed state in the cavity.

10 An object of the present invention is to provide a centrifuge of the type mentioned by way of introduction, which has a compact size and can easily be used for various types of separations by means of different container systems in the form of cassettes. Thus, the centrifuge can be used for separations and treatments where large amounts of liquid are to be handled in secondary containers, for instance in

15 connection with the washing of cells, as well as for separations of the type described in WO 95/01842. Further objects and advantages of the invention will be apparent from the following specification.

20 The inventive centrifuge is characterised in that the central compartment is a tubular shaft cavity in the centre of the rotor, and that the annular separation compartment is arranged around the cavity at the upper part thereof.

25 By this design of the rotor, large volumes of liquid in secondary containers can be held in the central compartment and the diameter of the rotor can still be made relatively small. The rotor obtains good balance by the placing of the liquids in the shaft cavity close to the axis of rotation of the rotor. Preferably the separation compartment has a conical shape and is inclined obliquely downwards or obliquely upwards, which further reduces the diameter of the rotor and expedites the separation through the inclined separation compartment.

30 The rotor is adapted to accommodate a container system comprising a tubular sleeve which is adapted to the shaft cavity of the rotor and on which the round bag is mounted and in which the secondary container/containers are arranged.

35 A first container system according to the invention, for separation and/or treatment of blood or blood components, adapted to be placed in the centrifuge, is characterised by a round bag which has an outer annular edge and an inner annular edge; two or

more flexible secondary containers, of which at least one contains a treatment liquid; a tube system connecting the round bag with the secondary containers; a tubular sleeve which is adapted to the shaft cavity of the rotor and which is adapted to accommodate the secondary containers standing side by side and resting against each other, and which at its upper part comprises a projecting flange, and in that the round bag, by means of its inner edge, is adapted to be mounted on said flange.

This container system is in the first place intended for separations and treatments comprising the handling of relatively large volumes of liquid in the secondary containers, for instance, when washing blood cells. In washing, use is made of one or more secondary containers containing washing liquid (washing liquid container) and an initially empty secondary container (waste liquid container) which is adapted to receive waste liquid which is displaced from the round bag after a completed washing step. The total volume of liquid in the secondary containers may constitute 2-3 litres. Thanks to the flexible secondary containers which rest against each other, the space is maximally utilised. In the course of the process, the volume of washing liquid in the washing liquid container decreases and increases to the same extent in the waste liquid container.

The container system is also suited for other types of separations and treatments which involve liquids in secondary containers, for instance, treating, reconditioning and preserving liquids, which at some stage of the process are transferred to other bags in the system to be mixed with a blood component therein. Even if use is not made of all bags during the actual centrifugation process, they must be loaded into the centrifuge since the containers normally constitute an interconnected sterile unit that should not be disconnected and be connected again.

A second container system according to the invention to be inserted in the centrifuge is characterised by a round bag having an outer annular edge and an inner annular edge; a secondary container; a tube connecting the round bag with the secondary container; a tubular sleeve which is adapted to accommodate the secondary container and which has a smaller diameter than the shaft cavity of the rotor and on its outside has support elements which are adapted to engage the walls of the cavity and centre the sleeve in the centre of the cavity, and at its upper part has a projecting flange, and in that the round bag by means of its inner edge is adapted to be mounted on said flange.

This container system makes it possible to use the same centrifuge also when relatively small volumes of liquid are to be handled in a secondary container in the central shaft cavity of the rotor, for instance, when only one initially empty container is 5 arranged in the sleeve to receive a separated component from the round bag while the centrifugation proceeds.

The invention will now be described in more detail with reference to the accompanying Figures.

10

Fig. 1 shows a section of an embodiment of a centrifuge according to the invention with a first container system inserted.

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Fig. 2 shows a section of an alternative embodiment of a centrifuge according to the invention with a second container system inserted.

Fig. 3 is a top plan view of a container system according to the invention.

Fig. 4 shows a section A-A of the container system according to Fig. 3.

20

Fig. 5 is a top plan view of a multiple bag.

Fig. 6 shows a section of a multiple bag according to Fig. 5, arranged in a sleeve and filled with liquid in two containers.

25

Fig. 7 shows a section of an alternative container system according to the invention.

The centrifuge according to Fig. 1 comprises a rotor 1 and its associated auxiliary equipment such as a drive system 2, a hydraulic system 3 and a control system for 30 the operation of the centrifuge (not shown), which is accommodated in an apparatus housing 4. The auxiliary equipment and the apparatus housing have been indicated schematically only.

The rotor has, concentrically with the axis of rotation of the rotor, an annular separation compartment 5 and a central tubular shaft cavity 6. The cavity 6 is relatively deep and narrow and extends vertically down in an enlarged rotor shaft. The rotor bowl 7 itself, which accommodates the separation compartment 5, surrounds the

cavity at the upper part thereof. A removable rotor lid 8 closes the separation compartment and the cavity and can in its central part be provided with a window 9 which permits inspection and photocell monitoring. The separation compartment has a conical shape and is inclined obliquely downwards, which results in a more 5 rapid separation and reduces the diameter of the rotor compared with a horizontally oriented compartment.

In the base of the separation compartment a flexible membrane 10 is arranged, which is clamped against the rotor bowl and defines a hydraulic compartment 11.

10 Thanks to the hydraulic system 3, a hydraulic liquid can be pumped through a duct 12 in the rotor shaft to the hydraulic compartment 11, the membrane 10 being expanded and reducing the volume of the separation compartment.

15 The rotor is specifically adapted to accommodate a container system in the form of a cassette comprising a tubular sleeve 17, which is adapted to the shaft cavity of the rotor and on which the round bag 13 is mounted and in which the secondary container/containers are arranged. Two different container systems to be inserted in the rotor are described in connection with Figs 3-7.

20 Fig. 2 shows an alternative embodiment of the centrifuge rotor according to the invention. Equivalent components in the different Figures have been given the same reference numerals. In the same way as in Fig. 1, the separation compartment 5 has a conical shape, but is in this case angled upwards. The separation compartment also has a more elliptic cross-section than the variant shown in Fig. 1.

25 A container system of the type which is described in more detail in connection with Fig. 7 is shown when arranged in the rotor. The rotor can, like the rotor in Fig. 1, be provided with the one or the other type of container system.

30 Figs 3 and 4 illustrate a container system according to the invention to be arranged in the centrifuge. Fig. 3 is a top plan view of the container system, and Fig. 4 shows a section A-A. The container system consists of a round bag 13, flexible secondary containers 14, 15, a tube system 16 connecting the round bag with the secondary containers, and a sleeve 17, in which the secondary containers are arranged standing side by side and resting against each other. The round bag 13 can be 35 made by two plastic films, arranged one above the other, being welded together along an outer annular edge 18 and an inner annular edge 19. In the example shown, the annular container 13 is cut off, and the opposite ends 20 and 21 so

formed are sealed and made to overlap one another, whereby the round bag obtains a conical shape in the same way as described in WO 95/01842. The welds of the round bag have been indicated by a dashed line inside the respective edge lines. The container system as shown is intended for washing blood cells and comprises two secondary containers, of which one is a washing liquid container 14 containing a washing liquid, e.g. a sterile aqueous solution of NaCl (0.9%) and glucose (0.2%), and the other is a waste container 15 which is initially empty. The sleeve 17 is adapted to be lowered into the shaft cavity 6 of the rotor (Figs 1 and 2) and may be made of, for instance, a plastic material which is sufficiently rigid to make the container system easy to handle. The sleeve has in its upper part a projecting flange 22, on which the round bag is mounted by means of its inner edge 19. The flange is provided with pins 23, which fit in corresponding holes 24 in welded-together portions of the round bag. The round bag is adapted to be accommodated by the annular separation compartment 5 of the rotor. The tube system 16 consists in the example shown of a tube 25 which is connected to the round bag close to the inner edge 19 thereof and which branches into a tube branch 26 which is connected to the washing liquid container 14, and a tube branch 27 which is connected to the waste container 15. The tube branch 26 is provided with a one-way valve 28, which allows only liquid flow from the washing liquid container to the round bag, and the tube branch 27 is provided with a one-way valve 29, which allows only liquid flow from the round bag to the waste container. The valves are normally closed and require a certain liquid pressure to open. Instead of these one-way valves, the tubes can be placed in pinch valves which are controlled by an automatic programme control in the centrifuge. The round bag is also provided with a tube 30, through which the blood cells are supplied to be washed or drawn off after washing.

The secondary containers are designed to be able to expand in the radial direction, such that each of them can fill the inner diameter of the sleeve and, in all positions, 30 yields good rotor balance. In centrifugation, the liquid in the secondary containers is pressed against the walls of the sleeve and the flexible containers must be able to adapt to this distribution of liquid.

When washing cells that have been treated according to the high glycerol method, 35 the initial washing steps must be carried out with a washing liquid of a higher salt concentration, in which case the sleeve 17 is correspondingly provided with three secondary containers, one of which is a washing liquid container containing a

hypertonic salt solution and one is a washing liquid container containing a physiological salt solution.

The sleeve can in a corresponding manner be provided with, for instance, an empty

5 secondary container which is adapted to receive a separated component from the round bag, and a secondary container which contains, for instance, a preservation liquid which after completion of the separation is supplied to the round bag and is mixed with a component remaining therein.

10 The secondary containers may consist of a multiple bag which is made by putting together and welding together a number of plastic films along the circumference, thereby forming containers between the films. Tube connections to the different spaces between the films are arranged in one edge of the multiple bag. Figs 5 and 6 illustrate an embodiment of a multiple bag 31 which is made by four joined film

15 layers 32 and which thus comprises three containers 33, 34 and 35 adjoining each other. Fig. 5 is a top plan view of the multiple bag with tube connections 36, 37 and 38 between the different film layers. Fig. 6 is a section of the multiple bag, two of the containers being filled with liquid and the multiple bag being arranged standing in a sleeve 17. For instance, the container 33 can be a washing liquid container

20 containing a physiological salt solution, the container 34 can be a washing liquid container containing a hypertonic salt solution, and the container 35 can be a waste container.

The function of the centrifuge and the container system will be described below with

25 reference to Fig. 1, the carrying out of the washing of blood cells being taken as an example. A container system of the type as shown in Figs 3 and 4 is used, one secondary container 14 containing washing liquid (washing liquid container), and the other 15 being initially empty (waste container). A batch of red blood cells that has been frozen and is mixed with glycerol is transferred to the round bag via a

30 tube 30. The container system is arranged in the rotor 1, and the rotor lid 8 is put on and locked. The centrifuge is operated for a predetermined period at a certain speed, whereby the major part of the glycerol is separated from the cells. The glycerol constitutes the lighter fraction and is collected adjacent to the centre of rotation against the inner edge 19 of the round bag. With a reduced speed of the rotor, a

35 predetermined volume of hydraulic fluid is pumped via the duct 12 to the hydraulic compartment 11, the membrane 10 being pressed into the separation compartment 5 and reducing its volume. The corresponding volume of glycerol is now pressed via

the tube 25 and the tube branch 27 to the waste container 15. The liquid pressure opens the one-way valve 29. Subsequently, the hydraulic pump is reversed and the same volume of hydraulic liquid as was previously pumped in is now sucked out of the hydraulic compartment 11, the corresponding volume of washing liquid being 5 sucked via the tube branch 28 and the tube 25 to the round bag. By reversals of the direction of rotation of the rotor, the washing liquid is mixed with the cells. Then the separation process is repeated, the consumed washing liquid being displaced to the waste container 15 and new washing liquid being sucked into the round bag. The washing cycle is repeated until the washing liquid is used up, and the cells are, 10 according to calculations, sufficiently cleaned from glycerol. The last batch of washing liquid is not separated but is used to resuspend the cells to a retransfusible form, and the cell slurry is transferred to a blood bag. During the centrifuging steps, the total volume of liquid in the sleeve 17 in the shaft cavity 6 of the rotor is constant since, in each step, the same volume of liquid is supplied to the waste 15 container 15 as is drawn off from the washing liquid container 14. The two secondary containers are made in such a manner that they are able to expand over the entire inner diameter of the sleeve, and the one container successively takes over the space of the other container during the process owing to their resting against each other. The rotor obtains good equilibrium, and it is possible to avoid great 20 stresses and the risk of breaking of the secondary containers.

Fig. 7 shows a section of a container system for separating blood components, which can be used in the same centrifuge as the system described above if only a small volume of liquid is to be held in the secondary container. Particularly, the 25 container system is intended to be used when only one separated component is to be received from the round bag. The container system differs from what has been described above in connection with Figs 3 and 4 by the tubular sleeve 39 having in this case a smaller diameter than the shaft cavity 6 of the rotor and having on its outside support elements 40 which are adapted to engage the walls of the cavity 30 and centre the sleeve in the centre of the cavity. The Figure shows an empty secondary container 41 standing in the sleeve 39. A tube 42 connects the secondary container with the round bag and connects at a point adjacent to the inner edge 19 of the round bag. The secondary container has a width which approximately corresponds to the inner circumference of half the sleeve and is arranged standing along 35 the sleeve wall as shown in the Figure. When being filled with liquid, it expands to a cylindrical shape which occupies the entire diameter of the sleeve. In the same way as described in connection with Figs 3-4, the round bag 13 can be made conical by

letting sealed opposite ends of the ring overlap. The conical angle can be directed upwards or downwards. Fig. 2 shows the container system mounted in a rotor, in which case a conical upward angling is used.

- 5 The container system is specifically suited for separations of sensitive cell suspensions which should not be exposed to high G fields for long periods. This is the case, for instance, when separating a thrombocyte suspension from combined buffycoat fractions from previous three-component separations of whole blood. A small rotor diameter and a secondary container which is centred at the axis of rotation of
- 10 the rotor then constitute a great advantage. The construction of the centrifuge allows the secondary container and its sleeve to be made high and narrow and be centred in a very low G field. The secondary container is suitably formed of a plastic film quality which is particularly suitable for storing a thrombocyte suspension. Such plastic films are known and designed to yield the necessary gas permeability etc.

Claims:

1. A centrifuge for separation and/or treatment of blood or blood components,
5 comprising a rotor (1) having a central compartment and an annular separation compartment (5), which are arranged concentrically with the axis of rotation of the rotor and are adapted to accommodate a container system comprising a round bag (13) and one or more secondary containers (14, 15, 31, 41) connected thereto, the separation compartment being adapted to accommodate the round bag and the
10 central compartment being adapted to accommodate the secondary containers, and the centrifuge comprising means (3, 10, 11, 12) for reducing, in operation, the volume of the separation compartment in order to displace a separated component from the round bag to a secondary container in the central compartment, characterised in that the central compartment is a tubular shaft cavity (6) in the centre of the
15 rotor, and that the separation compartment (5) is arranged around said cavity at the upper part thereof.

2. A centrifuge as claimed in claim 1, characterised in that the rotor is adapted to accommodate a container system comprising a tubular sleeve (17, 39) which is
20 adapted to the shaft cavity of the rotor and on which the round bag is mounted and in which the secondary container/containers are arranged.

3. A centrifuge as claimed in claim 1, characterised in that the separation compartment (5) has a conical shape and is inclined obliquely upwards.
25

4. A centrifuge as claimed in claim 1, characterised in that the separation compartment (5) has a conical shape and is inclined obliquely downwards.

5. A container system for separation and/or treatment of blood or blood components, adapted to be placed in a centrifuge as claimed in claim 1, characterised by
30 a round bag (13) having an outer annular edge (18) and an inner annular edge (19); two or more flexible secondary containers (14, 15), of which at least one contains a treatment liquid;
a tube system (16) connecting the round bag with the secondary containers;
35 a tubular sleeve (17) which is adapted to the shaft cavity of the rotor and which is adapted to accommodate the secondary containers standing side by side and

resting against each other, and which at its upper part comprises a projecting flange (22), and in

that the round bag (13), by means of its inner edge (19), is adapted to be mounted on said flange.

5

6. A container system as claimed in claim 5, characterised in that the secondary containers consist of a multiple bag (31), which is formed of flexible sheets of plastic film (32), which have been arranged on top of each other and welded together along the circumference, thereby forming containers (33-35) adjoining each other.

10

7. A container system as claimed in claim 5, characterised in that the tube system consists of a tube (25), which is connected to the round bag close to the inner edge thereof and which branches into a tube branch to each of the secondary containers.

15

8. A container system as claimed in claim 5, characterised in that at least one secondary container (14, 33, 34) contains washing liquid for blood cells, and that at least one secondary container (15, 35) is initially empty and adapted to receive waste liquid which is displaced from the round bag after washing of blood cells.

20

9. A container system as claimed in claim 8, characterised in that two secondary containers (33, 34) contain washing liquid, one (34) containing a hypertonic salt solution and the other (33) containing a physiological salt solution.

25

10. A container system for separating blood components, adapted to be placed in a centrifuge as claimed in claim 1, characterised by a round bag (13) having an outer annular edge (18) and an inner annular edge (19);

a secondary container (41);

a tube (42) connecting the round bag with the secondary container;

a tubular sleeve (39) which is adapted to accommodate the secondary container

30

(41) and which has a smaller diameter than the shaft cavity (6) of the rotor and on its outside has support elements (40) which are adapted to engage the walls of the cavity and centre the sleeve in the centre of the cavity, and at its upper part has a projecting flange (22), and in

that the round bag (13) by means of its inner edge (19) is adapted to be mounted

35

on said flange.

11. A container system as claimed in claim 10, characterised in that it is intended for separation of a thrombocyte suspension from combined buffycoat fractions from previous three-component separations of whole blood, and that the secondary container (41) is made of a plastic film quality which is particularly suited for storing a
5 thrombocyte suspension.

1 / 4

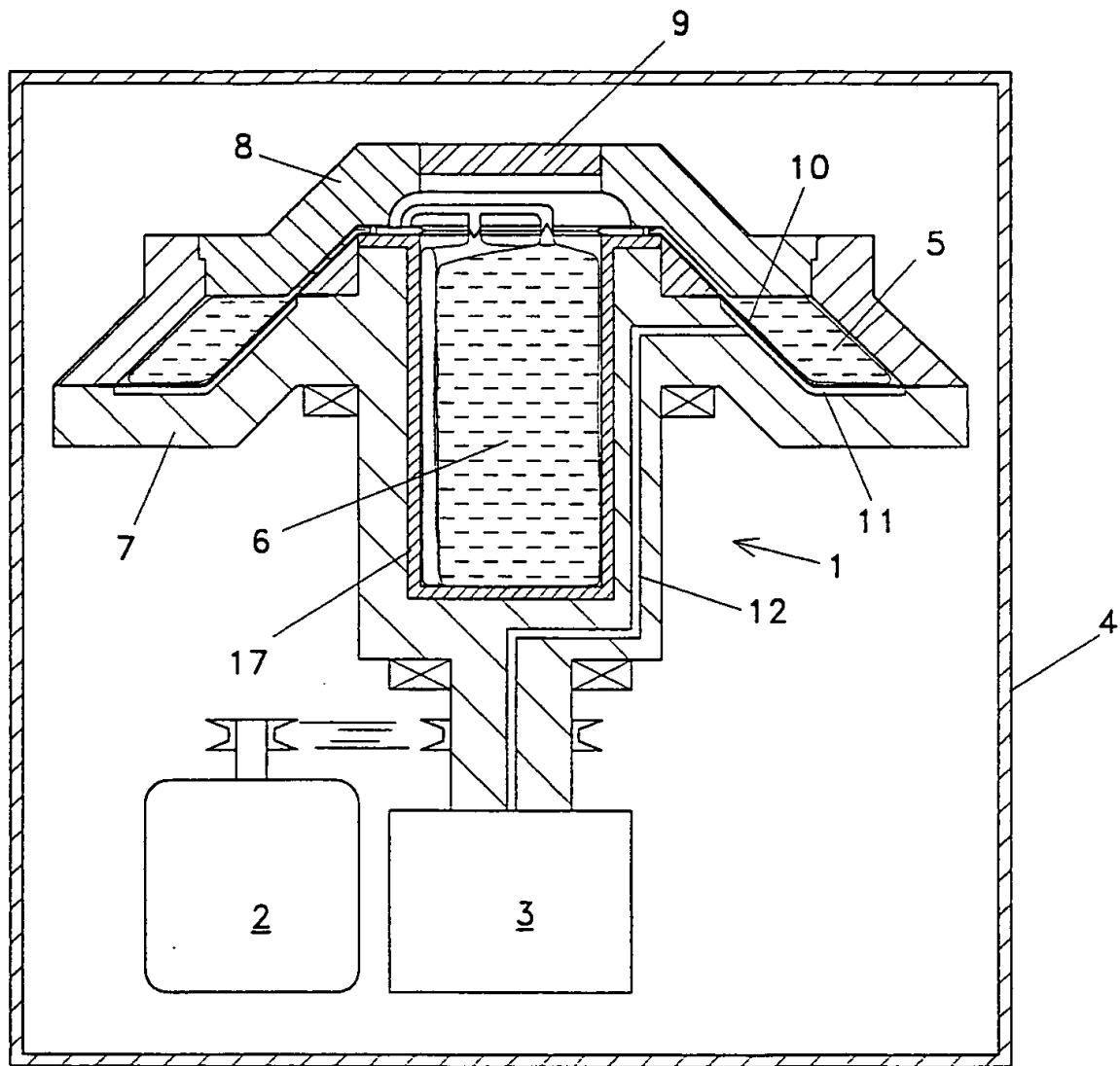


Fig 1

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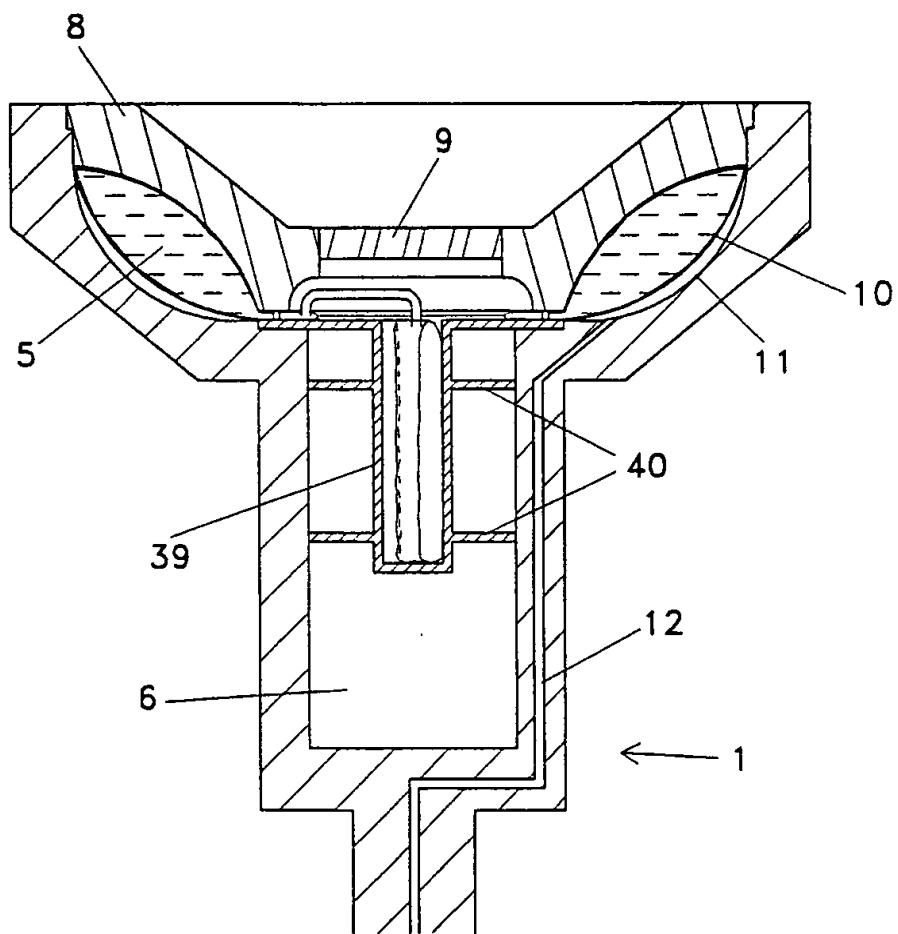


Fig 2

3/4

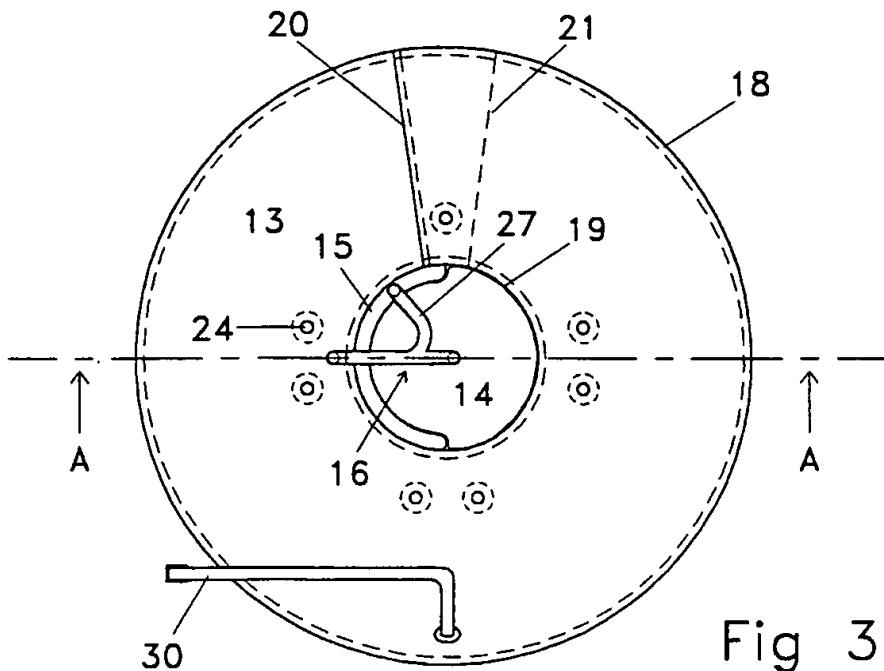


Fig 3

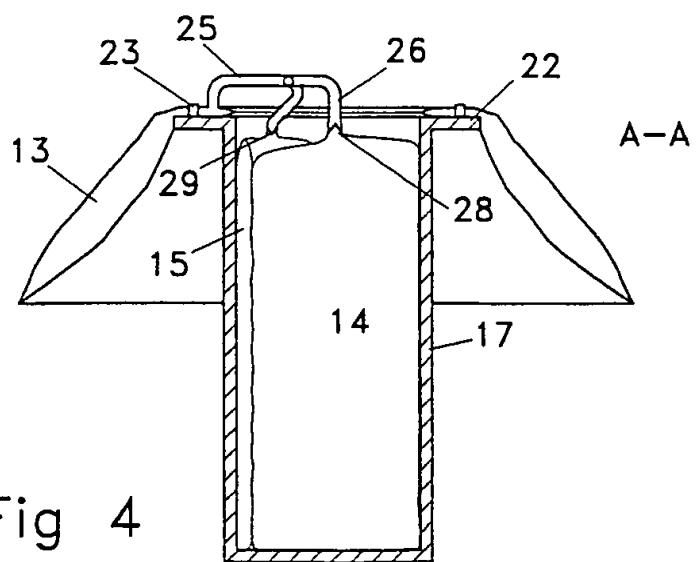


Fig 4

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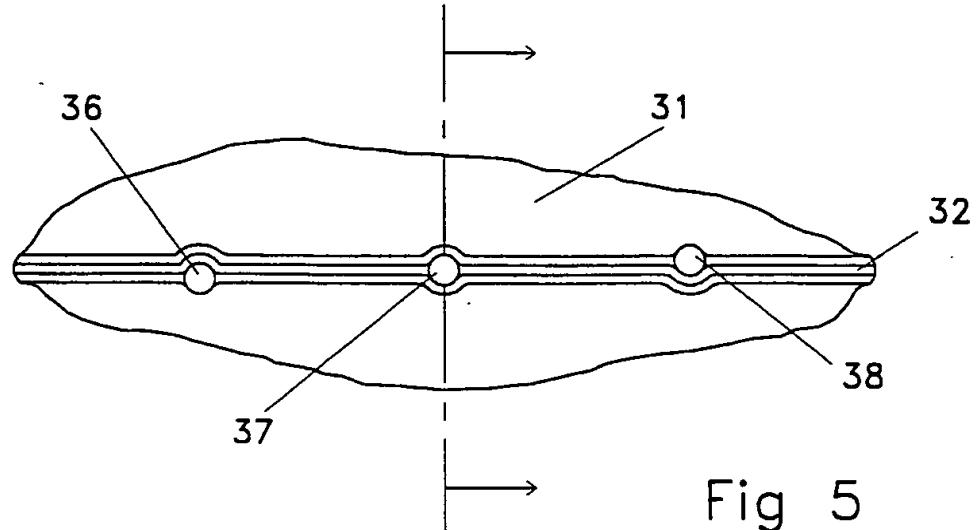


Fig. 5

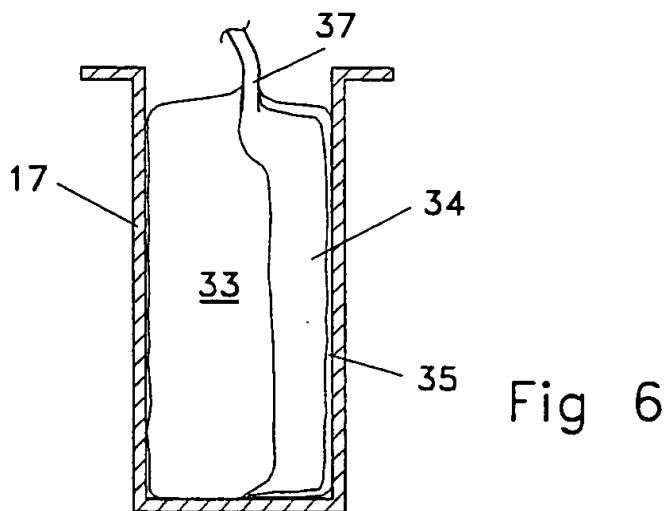
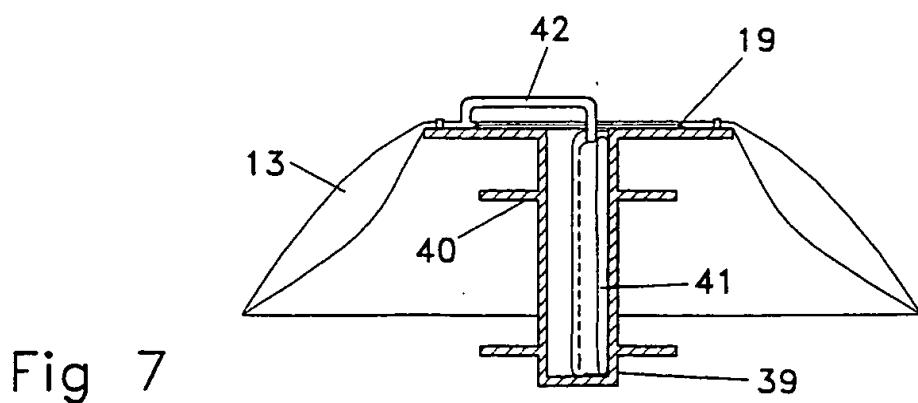


Fig. 6



INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 98/00246

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: B04B 5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K, A61L, B04B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5114396 A (PETER UNGER ET AL), 19 May 1992 (19.05.92), column 2, line 65 - column 4, line 52, figures 1-3 --	1-11
A	WO 8706857 A1 (OMEGA MEDICINTEKNIK AB), 19 November 1987 (19.11.87), figure 1, abstract --	1-11
A	US 3987961 A (HARTMUT SINN ET AL), 26 October 1976 (26.10.76), figure 1, abstract --	1-11

 Further documents are listed in the continuation of Box C. See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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26 May 1998	29-05-1998
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 9501842 A1 (OMEGA MEDICINTEKNIK AB), 19 January 1995 (19.01.95), figure 7, abstract -----	1-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

29/04/98

International application No.

PCT/SE 98/00246

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